

**In the claims:**

Applicants present all pending claims with status indicator in compliance with the practice guidelines for making amendments under 37 C.F.R. §1.121(c) (1).

Please cancel claims 24-26, 28-29, 31-32 and 53, without prejudice to pursue the subject matter of these claims in the subject application at a later time.

Please amend claims 1, 3, 9, 17, 30, 34, 35, 50, 52, 55 and 56 and add new claims 57-63 as follows:

1. (Currently amended) A method of inhibiting rejection of a solid organ or tissue/cellular transplant in a subject ~~having a transplanted tissue comprising:~~
  - a) administering T cell depleted bone marrow cells to the subject before, during and/or after a solid organ or tissue/cellular transplant; an alkylating agent to the subject; and
  - b) subsequently administering an alkylating agent to the subject in an amount that facilitates mixed hematopoietic chimerism; T-cell depleted bone marrow cells to the subject before, during or after the solid organ or tissue/cellular transplant, thereby inhibiting rejection of the solid organ or tissue/cellular transplant and
  - c) administering to the subject an immunosuppressive composition before, during and/or after the transplant, which immunosuppressive composition blocks T cell costimulatory signals in the subject;  
thereby inhibiting rejection of the solid organ or tissue/cellular transplant.
2. (Original) The method of claim 1, wherein the alkylating agent is busulfan.

3. (Currently amended) The method of claim 1 further comprising the step of ~~administering to the subject an immunosuppressive composition that blocks T cell costimulatory signals in the subject]~~ a second administration of T cell depleted bone marrow cells to the subject after step (b).
4. (Original) The method of claim 3, wherein the immunosuppressive composition comprises a combination of a first ligand that interferes with binding of CD28 to either CD80 or CD86, and a second ligand that interferes with binding of CD154 to CD40.
5. (Original) The method of claim 4, wherein the first ligand is a soluble CTLA4 molecule.
6. (Previously presented) The method of claim 4, wherein the first ligand is a CTLA4Ig.
- 7-8. (Canceled)
9. (Currently amended) A method for establishing mixed hematopoietic chimerism in a subject so as to inhibit or reduce rejection of a solid organ or tissue/cellular transplant, comprising:
  - a) administering T cell depleted bone marrow cells to a subject having a solid organ or tissue/cellular transplant;
  - b) administering an alkylating agent to the subject after step (a), in an amount that facilitates mixed hematopoietic chimerism; and
  - c) administering an immunosuppressive composition that blocks T cell costimulatory signals in the subject before, during and/or after the transplant,

thereby establishing hematopoietic chimerism in the subject so as to inhibit or reduce rejection of the solid organ or tissue/cellular transplant.

10. (Original) The method of claim 9, wherein the alkylating agent is busulfan.
11. (Withdrawn) The method of claim 9, wherein the immunosuppressive composition comprises a combination of a first ligand that interferes with binding of CD28 to either CD80 or CD86, and a second ligand that interferes with binding of CD154 to CD40.
12. (Original) The method of claim 11, wherein the first ligand is a soluble CTLA4 molecule.
13. (Previously presented) The method of claim 11, wherein the first ligand is a CTLA4Ig.
- 14-16. (Canceled)
17. (Currently amended) The method of claim 9 further comprising the step of administering to the subject a second administration of T cell depleted bone marrow cells to the subject after step (b), wherein the T cell depleted bone marrow is administered in at least two doses.
- 18-29. (Canceled)
30. (Currently amended) The method of claim 2 or 10, wherein the busulfan is administered within any of (a) one day 24 hours prior to the solid organ or tissue/cellular transplant, (b) twelve hours prior to the solid organ or

tissue/cellular transplant, or (c) six hours prior to the solid organ or tissue/cellular transplant.

31-32. (Canceled)

33. (Previously presented) The method of claim 1 or 9, wherein the transplanted tissue is a skin graft.

34. (Currently amended) A method of reducing rejection of a solid organ or tissue/cellular transplant in a subject in need thereof comprising:

- a) administering a first dose of T cell depleted bone marrow cells and an immunosuppressive composition to a subject;
- b) placement of an organ or tissue/cellular transplant to the subject before, during and/or after the administration of the immunosuppressive composition;
- c) administering busulfan to the subject in an amount that facilitates mixed chimerism; and
- d) administering a second dose of T cell depleted bone marrow cells and an immunosuppressive ~~agent-composition~~,

thereby reducing rejection of the solid organ or tissue/cellular transplant.

35. (Currently amended) The method of claim 34, wherein the immunosuppressive ~~agent-composition~~ is a combination of a first ligand that interferes with binding of CD28 to either CD80 or CD86, and a second ligand that interferes with binding of CD154 to CD40.

36. (Original) The method of claim 35, wherein the first ligand is a soluble CTLA4 molecule.

37. (Previously presented) The method of claim 35, wherein the first ligand is a CTLA4Ig.
- 38-43. (Canceled)
44. (Previously presented) The method of claim 5, 12, or 36, wherein the soluble CTLA4 molecule comprises an extracellular domain of CTLA4 which binds a B7 antigen.
45. (Previously presented) The method of claim 44, wherein the extracellular domain of CTLA4 has an amino acid sequence which begins with methionine at position 27 and ends with aspartic acid at position 150 as shown in SEQ ID NO:14, or which begins with alanine at position 26 and ends with aspartic acid at position 150 as shown in SEQ ID NO:14.
46. (Previously presented) The method of claim 6, wherein the CTLA4Ig comprises an amino acid sequence which begins with methionine at position 27 and ends with lysine at position 383 as shown in SEQ ID NO:14, or which begins with alanine at position 26 and ends with lysine at position 383 as shown in SEQ ID NO:14.
47. (Previously presented) The method of claim 5, 12, or 36, wherein the soluble CTLA4 molecule is a soluble CTLA4 mutant molecule.
48. (Previously presented) The method of claim 46, wherein the soluble CTLA4 mutant molecule comprises a mutated extracellular domain of CTLA4 which binds a B7 antigen.

49. (Previously presented) The method of claim 48, wherein the mutated extracellular domain of CTLA4 has an amino acid sequence which begins with methionine at position 27 and ends with aspartic acid at position 150 as shown in SEQ ID NO:4, or which begins with alanine at position 26 and ends with aspartic acid at position 150 as shown in SEQ ID NO:4.
50. (Currently Amended) The method of claim 47, wherein the soluble CTLA4 mutant molecule is ~~L104EA29Y1g comprising~~ comprises an amino acid sequence which begins with methionine at position 27 and ends with lysine at position 383 as shown in SEQ ID NO:4, or which begins with alanine at position 26 and ends with lysine at position 383 as shown in SEQ ID NO:4.
51. (Previously presented) The method of claim 4, 11 or 35, wherein the second ligand is a ligand for CD40.
52. (Currently amended) The method of claim 44 51, wherein the ligand for CD40 is an anti-CD40 antibody.
53. (Canceled)
54. (Previously presented) The method of claim 4, 11 or 35, wherein the first ligand is a soluble CTLA4 molecule and the second ligand is an anti-CD40 Ab.
55. (Currently amended) A method of inhibiting rejection of a solid organ or tissue/cellular transplant in a subject ~~having a transplanted tissue comprising~~
  - a) administering T cell depleted bone marrow cells to the subject;

- b) subsequently administering busulfan to the subject in an amount that facilitates mixed hematopoietic chimerism; and
  - c) administering CTLA4Ig and an anti-CD40 antibody to the subject before, during and/or after the solid organ or tissue/cellular transplant,  
thereby inhibiting rejection of the solid organ or tissue/cellular transplant.
56. (Currently amended) A method of inhibiting rejection of a solid organ or tissue/cellular transplant in a subject having a transplanted tissue comprising
- a) administering T cell depleted bone marrow cells to a subject;
  - b) subsequently administering busulfan to the subject in an amount that facilitates mixed hematopoietic chimerism ; and
  - c) administering L104EA29YIg—a soluble CTLA4 mutant molecule comprising an amino acid which begins with methionine at position 27 and ends with lysine at position 383 as shown in SEQ ID NO:4, or which begins with alanine at position 26 and ends with lysine at position 383 as shown in SEQ ID NO:4 and an anti-CD40 antibody to the subject before, during and/or after the solid organ or tissue/cellular transplant,  
thereby inhibiting rejection of the solid organ or tissue/cellular transplant.

Please add new claims 57-63 as follows:

57. (New) The method of claim 1 or 9, wherein the amount of an alkylating agent that facilitates mixed hematopoietic chimerism is an amount selected from any of 4 mg/kg weight of the subject, 10 mg/kg weight of the subject, 20 mg/kg weight of the subject, 30 mg/kg weight of the subject, between 4-16 mg/kg weight of the subject, or between 0.1 to 20 mg/kg weight of the subject.

58. (New) The method of claim 34, 55, or 56, wherein the amount of an busulfan that facilitates mixed hematopoietic chimerism is an amount selected from any of 4 mg/kg weight of the subject, 10 mg/kg weight of the subject, 20 mg/kg weight of the subject, 30 mg/kg weight of the subject, between 4-16 mg/kg weight of the subject, or between 0.1 to 20 mg/kg weight of the subject.
59. (New) The method of claim 1 or 9, wherein the amount of the alkylating agent that facilitates mixed hematopoietic chimerism is an amount below the LD<sub>50</sub> dose of 136 mg/kg.
60. (New) The method of claim 34, 55, or 56, wherein the amount of busulfan that facilitates mixed hematopoietic chimerism is an amount below the LD<sub>50</sub> dose of 136 mg/kg.
61. (New) The method of claim 55 or 56 further comprising the step of administering to the subject a second administration of T cell depleted bone marrow cells to the subject after step (b).
62. (New) A method of reducing rejection of a solid organ or tissue/cellular transplant in a subject in need thereof comprising:
  - a) administering a first dose of T cell depleted bone marrow cells to the subject;
  - b) administering an immunosuppressive composition that blocks T cell costimulatory signals in the subject before, during or after the solid organ or tissue/cellular transplant;
  - c) administering busulfan to the subject subject in an amount below the LD<sub>50</sub> dose of 136 mg/kg; and



d) administering a second dose of T cell depleted bone marrow cells to the subject,  
thereby reducing rejection of the solid organ or tissue/cellular transplant.

63. (New) A method of inhibiting rejection of a solid organ or tissue/cellular transplant in a subject having a transplanted tissue comprising:

- a) administering T cell depleted bone marrow cells to the subject;
- b) subsequently administering an alkylating agent to the subject in an amount below the LD<sub>50</sub> dose of 136 mg/kg;
- c) administering T cell depleted bone marrow cells to the subject; and
- d) administering to the subject an immunosuppressive composition that blocks T cell costimulatory signals in the subject before, during or after the transplant.